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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,965	09/14/2005	Tim Bowden	1510-1102	7978

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EXAMINER	
DICKINSON, PAUL W	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
07/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,965	BOWDEN ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *8,9,13-17,21-28 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-12,18,29 and 31* is/are rejected.

7)☒ Claim(s) *19-20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 3/31/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant submits new Claims 29-31. Claim 30 is directed to a polymer wherein the terminal functional group is a carboxylate and the polyester is polymerized from trimethylene carbonate. This compound is not encompassed by the election of species of phosphatidyl choline as the terminal functional group and a polyester that is polymerized from trimethlyene carbonate. Claim 30 is therefore withdrawn by original presentation.

Response to Arguments

Election/Restrictions

The Examiner required restriction between Group I (Claims 1-12 and 18-28), Group II (Claims 13-16), and Group III (Claim 17). Applicant provisionally elected Group I with traverse.

Applicant argues that the instant invention is not anticipated by Kim et al (Journal of Polymer Science: Part A: Polymer Chemistry, 2001), and therefore lack of a special technical feature has not been demonstrated. Applicant argues that Kim et al discloses polymers having a phosphate end group and a polyester chain but does not disclose a

phospholipid end group as claimed. Applicant provides examples of phospholipids and argues that a phospholipid group is not the equivalent to a phosphate group in that if one replaced the polar phospholipid end group with a non-polar phosphate group, the polymer would not be amphiphilic nor produce micelles or vesicles. Further, a phosphate group would also not provide sufficient bioavailability for drug delivery. Applicant cites the specification to show disclosure of three specific phospholipid groups and an example containing a phosphatidyl choline group. Further, Kim et al does not provide evidence that a polyester combined with a phospholipid is known.

Applicant's arguments have been fully considered but are not found persuasive. Applicant's claimed invention is directed to a polymer compound comprising at least one biodegradable polyester having a terminal functional group based on hydrophilic moieties of phospholipids. The phrase "functional groups based on hydrophilic moieties of phosopholipids" is unclear and this genus encompasses a myriad of possible groups (see ***Claim Rejections - 35 USC § 112*** below). The Examiner is taking the broadest reasonable interpretation of this phrase, which encompasses the compounds disclosed by Kim et al described in the previous office action.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

Claims 1-7 and 10-12 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant argues that the phrase "functional group based on hydrophilic moieties of phospholipids" is not vague and indefinite. The examples provided in the specification serve as a definition of this term. Furthermore, Applicant provides examples for what phospholipids are.

Applicant arguments have been fully considered but are not found persuasive. The examples provided are not limiting. "Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993)" MPEP § 2145, VI. As stated in the previous office action, it is unclear how far a functional group based on said hydrophilic moieties can deviate from the parent compound without it being so far removed therefrom as to be a completely different compound.

The rejection of Claims 1-7 and 10-12 under 35 U.S.C. 112, second paragraph, is maintained.

Claim Rejections - 35 USC § 102

Claims 1, 4-7, and 10-11 were rejected under 35 U.S.C. 102(a) as being anticipated by Lucke et al (Pharmaceutical Research, 2002). Claims 2 and 12 were rejected under 35 U.S.C. 102(b) as being anticipated by Hecht et al (J. Am. Chem. Soc., 1999). Claim 3 was rejected under 35 U.S.C. 102(b) as being anticipatd by Burt et al (Colloids and Surfaces B: Biointerfaces, 1999).

Applicant argues that the instant invention is patentably distinct from the above references. Applicant argues that the specification provides three examples of terminal

groups. Further, Applicant provides text book examples of natural phospholipids. Applicant describes each reference and explains how it is distinguished from the claimed invention. Applicant argues that carboxylic acids (Luck et al), coumarin (Hecht et al), nor methoxypolyethylene glycol" would not be considered hydrophilic moieties of phospholipids. Further, Applicant argues that the above references do not disclose phospholipid moieties.

Applicant's arguments have been fully considered but are not found persuasive. The Examiner must give the claims their broadest reasonable interpretation. Webster's Nineth New Collegiate Dictionary defines a moiety as "one of the portions into which something is divided". The Examiner is interpreting hydrophilic moieties of phospholipids as any hydrophilic group that could be part of the structure of a phospholipid. Carboxylic acids, coumarin, and methoxypolyethylene glycol are hydropholic groups that could be part of the structure of a phospholipid. Regarding coumarin, Applicant argues that there are no known natural phospholipid structures that contain a coumarin skeleton and further, the terminal group preferably comprises one or more charged groups. There is nothing in the claims, however, that limit the phospholipids to natural structures nor a requirement that the terminal groups be charged. Furthermore, the as-filed application contemplated carboxylic acid, carboxylates, phophonic acid, phosphate, sulphonate, sulphonic acid, peptides, nucleotides, and carbohydrates as possible functional groups based on hydrophilic moieties of phospholipids (see original Claim 7).

Claim 7 is now amended to limit the functional group to phosphatidyl choline, phosphatidyl ethanolamine, or phosphatidyl serine.

The rejection of Claim 7 under 35 U.S.C. 102(a) as being anticipated by Lucke et al is withdrawn. The rejection of Claims 1, 4-6, and 10-11 under 35 U.S.C. 102(a) as being anticipated by Lucke et al is maintained. The rejection of Claims 2 and 12 under 35 U.S.C. 102(b) as being anticipated by Hecht et al is maintained. The rejection of Claim 3 under 35 U.S.C. 102(b) is maintained.

Claim Rejections - 35 USC § 103

Claim 2 was rejected under 35 U.S.C. 103(a) as being unpatentable over WO 0056802.

Applicant argues that the instant invention is patentably distinct from the above reference. Applicant argues that the reference discloses hyperbranched polymer structures and based on non-degradable polyether linkages. Further functionalization with lactones provides linear degradable polyester fragments.

Applicant's argument have been fully considered but are not found persuasive. The reference does not disclose that the hyperbranched polymer is not degradable. In contrast, it indicates that it is susceptible to hydrolysis (see page 2, first full paragraph)

The rejection of Claim 2 under 35 U.S.C. 103(a) as being unpatentable over WO 0056802 is maintained.

Claim 18 was rejected under 35 U.S.C. 103(a) as being unpatentable over US 6166173 ('173) in view of Kim et al (Journal of Polymer Science: Part A: Polymer Chemistry, 2001).

Applicant argues the proposed combination of the above references would not result in the claimed invention. '173 discloses step-growth polymerization that results in phosphates at varied places along the polymer backbone. In contrast, the present invention describes how the end groups of these polymers can be functionalized with phosphates. In so doing, micelles can be formed. In the instant invention, the functional group is charged. '173 does not describe charged groups nor phospholipid end groups. Further, the polymers disclosed by '173 would not form micelles and the reference does not mention or describe micelles. While Kim et al present a way of synthesizing biodegradable initiators containing phosphate end groups, the phosphate end groups are not of ionic structure and one would realize that the resulting polymer would not create micelles. Further, the instant invention is directed to a fully biodegradable polymer, whereas the polymer presented by Kim et al is only partly biodegradable and the rest non-biodegradable.

Applicants arguments have been fully considered but are not found persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in

the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the references would be combined to provide improved macromolecular architectures.

In response to applicant's argument that the references fail to show certain features of applicant's invention, the features upon which applicant relies are not recited in the rejected claim. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claim 18 does not require a terminal phospholipid group, but a terminal group based on a phospholipid, and specifically, a phosphate. Claim 18 does not require a charged functional group. Claim 18 does not require the polyester to be formed into a micelle.

For the reasons as stated in the record, it would be obvious to make a polymer as disclosed by '173 wherein the polymer has a functionalized end, thus providing the instantly claimed invention.

The rejection of Claim 18 under 35 U.S.C. 103(a) as being unpatentable over US 6166173 in view of Kim et al is maintained.

New Grounds of Rejection

Specification

The amendment filed 3/31/2008 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material

which is not supported by the original disclosure is as follows: the Appendix to the Specification filed 3/31/2008.

Applicant is required to cancel the new matter in the reply to this Office Action.

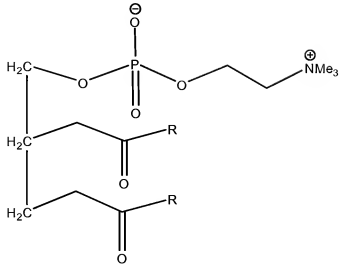
Claim Rejections - 35 USC § 112 – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

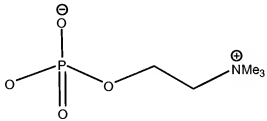
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

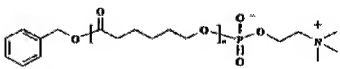
Phosphatidyl choline, phosphatidyl serine, and phosphatidyl ethanolamine are phospholipids. A phosphatdiyl choline, for example, has the following structure:



Where R is a saturated or unsaturated hydrocarbon. It is unclear how this class of compounds could serve as a terminal group, where the point of attachment would be, etc. The specification does not disclose how phosphatidyl choline could serve as a functional group. The specification does disclose the following functional group:



which is covalently bonded to a polyester:



(see Figure 1). Although this is reasonably a fragment of a phosphatidyl choline, it is not a phosphatidyl choline. The specification provides no guidance that would allow one of skill in the art to determine how a phosphatidyl choline nor the other disclosed phosphatidyl compounds could serve as a functional group.

***Claim Rejections - 35 USC § 112 - Lack* of Enablement**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for biodegradable polyesters having phosphatidyl choline, phosphatidyl serine, and phosphatidyl ethanolamine as terminal functional groups. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to prepare such compounds of the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to biodegradable polyesters having terminal functional

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not

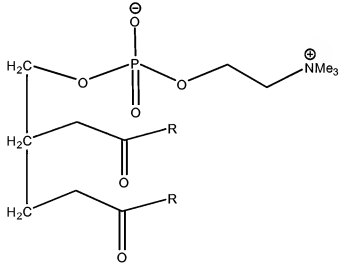
groups. The relative skill of those in the art is high, that of an MD or PhD. That factor is outweighed, however, by the unpredictable nature of the art.

2. The breadth of the claims

The claim is directed to using phosphatidyl choline, phosphatidyl serine, and phosphatidyl ethanolamine as a terminal functional groups.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for how phosphatidyl choline, phosphatidyl serine, or phosophatidyl ethanolamine could serve as a functional group. The structure of a phosphatidyl choline, for example, is:



Wherein R is a saturated or unsaturated alkyl group. This phospholipid would

"experimentation".

have to be chemically modified to covalently bond to a polyester. It cannot, therefore, serve as a functional group itself as there is no reasonable point of attachment without further modification, such as cleaving a bond between an oxygen and methylene carbon, at which point it would no longer be a phosphatidyl choline.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that phosphatidyl choline, phosphatidyl serine, and phosphatidyl ethanolamine could serve as functional groups as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "functional group based on hydrophilic moieties of phospholipids" in Claim 1 is vague and indefinite. It is unclear what

compounds/fragments "hydrophilic moieties of phospholipids" encompasses. There is no limiting definition of this term in the specification. Furthermore, it is unclear how far a functional group based on said hydrophilic moieties can deviate from the parent compound without it being so far removed therefrom as to be a completely different compound.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by US 4698099 ('099). '099 discloses a compound of the formula

Where at least one R group is a biodegradable polyester and at least one of the remaining two R groups is cationic (see abstract; col 1, lines 37-55; col 2, line 67 to col 4, line 15; Claims 1-6). The resulting phosphate is a charged polar head of a phospholipid with a functional group.

Allowable Subject Matter

Claims 19-20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

July 8, 2008